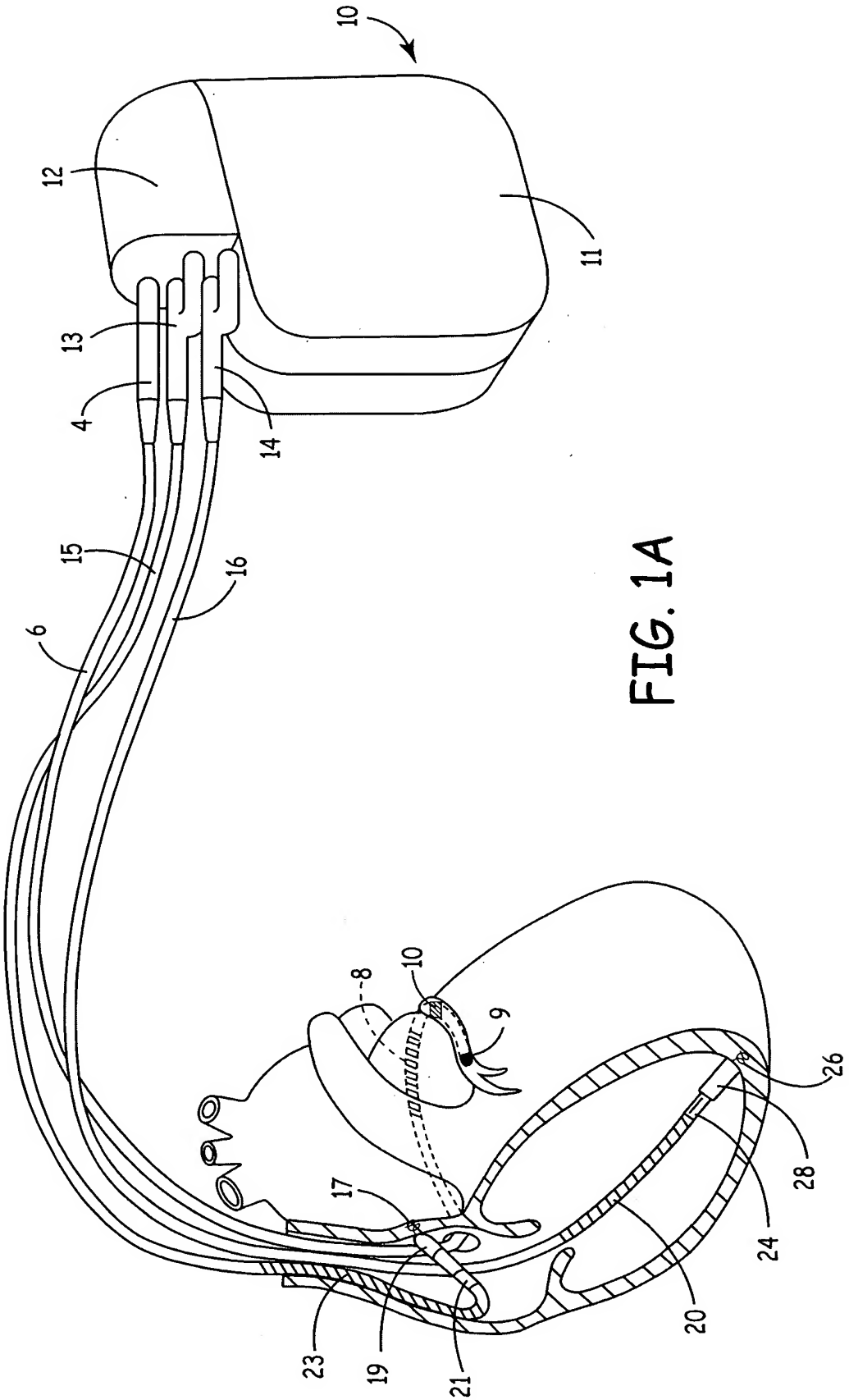


FIG. 1A

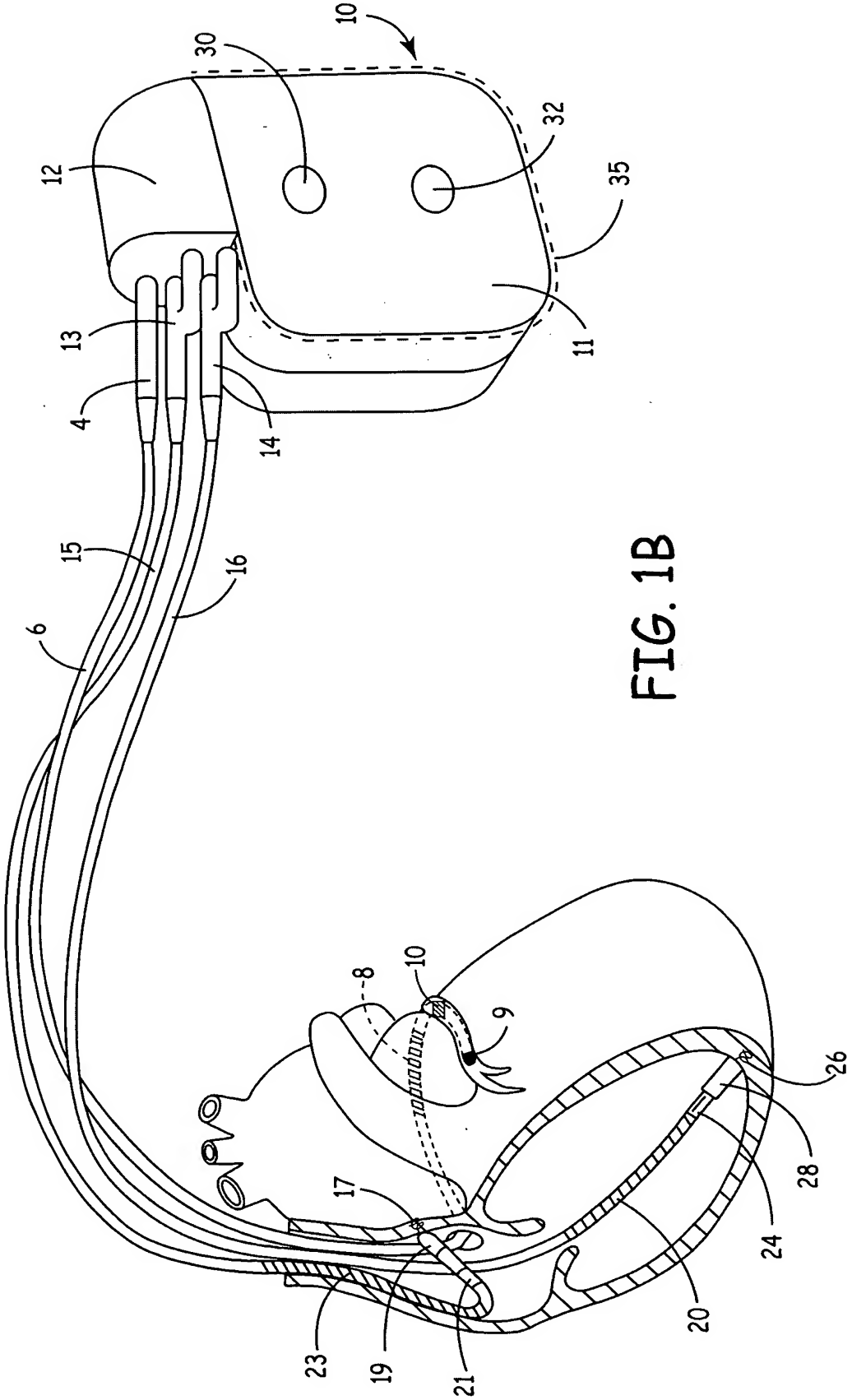


FIG. 1B

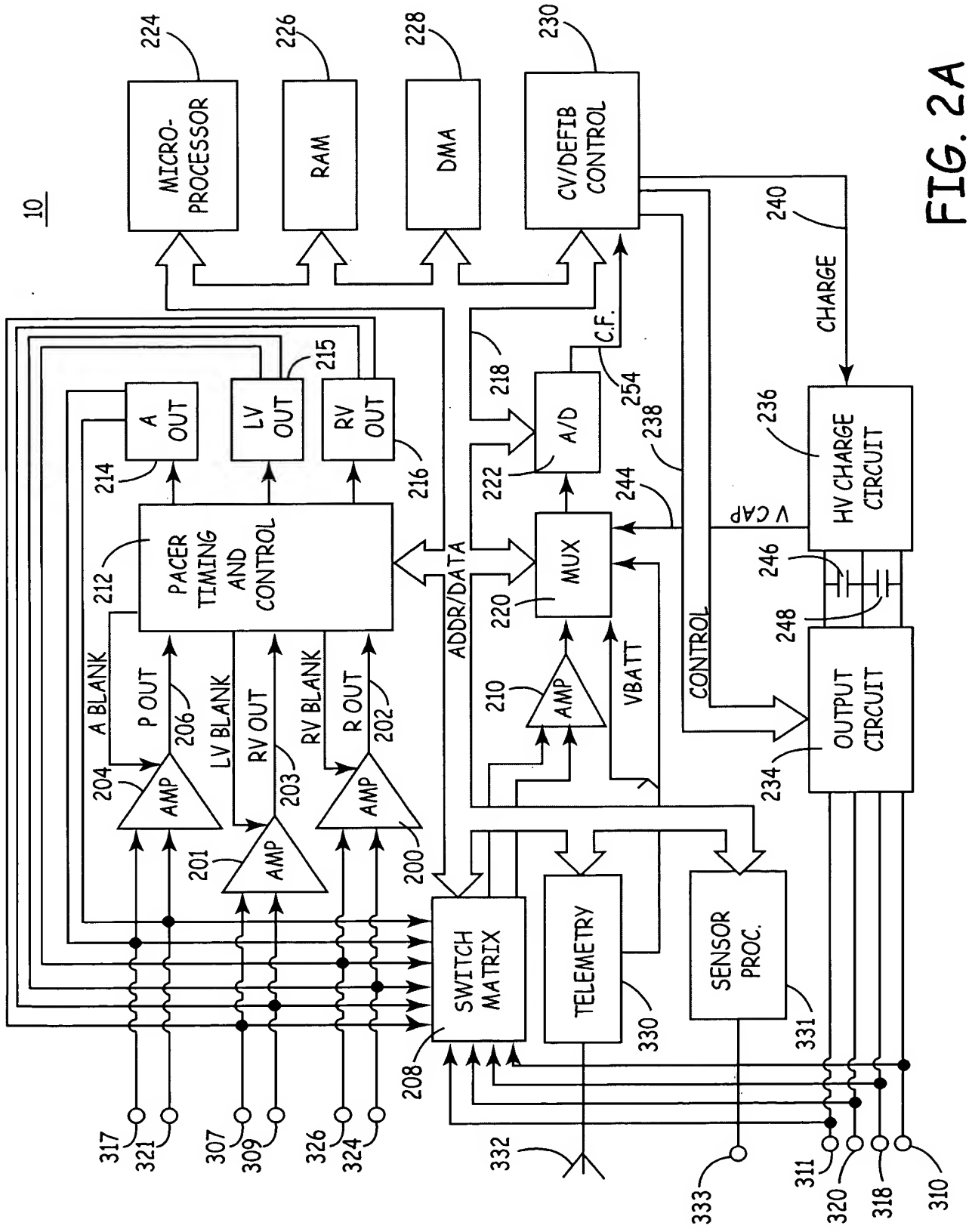

10
MICRO-PROCESSOR
224
RAM
226
DMA
228
CV/DEFIB CONTROL
230
240
CHARGE
C.F.
254
218
A/D
222
238
236
HV CHARGE CIRCUIT
V CAP
246
248
OUTPUT CIRCUIT
234
CONTROL
244
MUX
220
ADDR/DATA
PACER TIMING AND CONTROL
212
A OUT
214
LV OUT
215
RV OUT
216
A BLANK
P OUT
206
LV BLANK
RV OUT
RV BLANK
R OUT
202
204
AMP
203
201
200
210
VBATT
SWITCH MATRIX
208
TELEMETRY
330
SENSOR PROC.
331
332
333
317
321
307
309
326
324
311
320
318
310

FIG. 2A

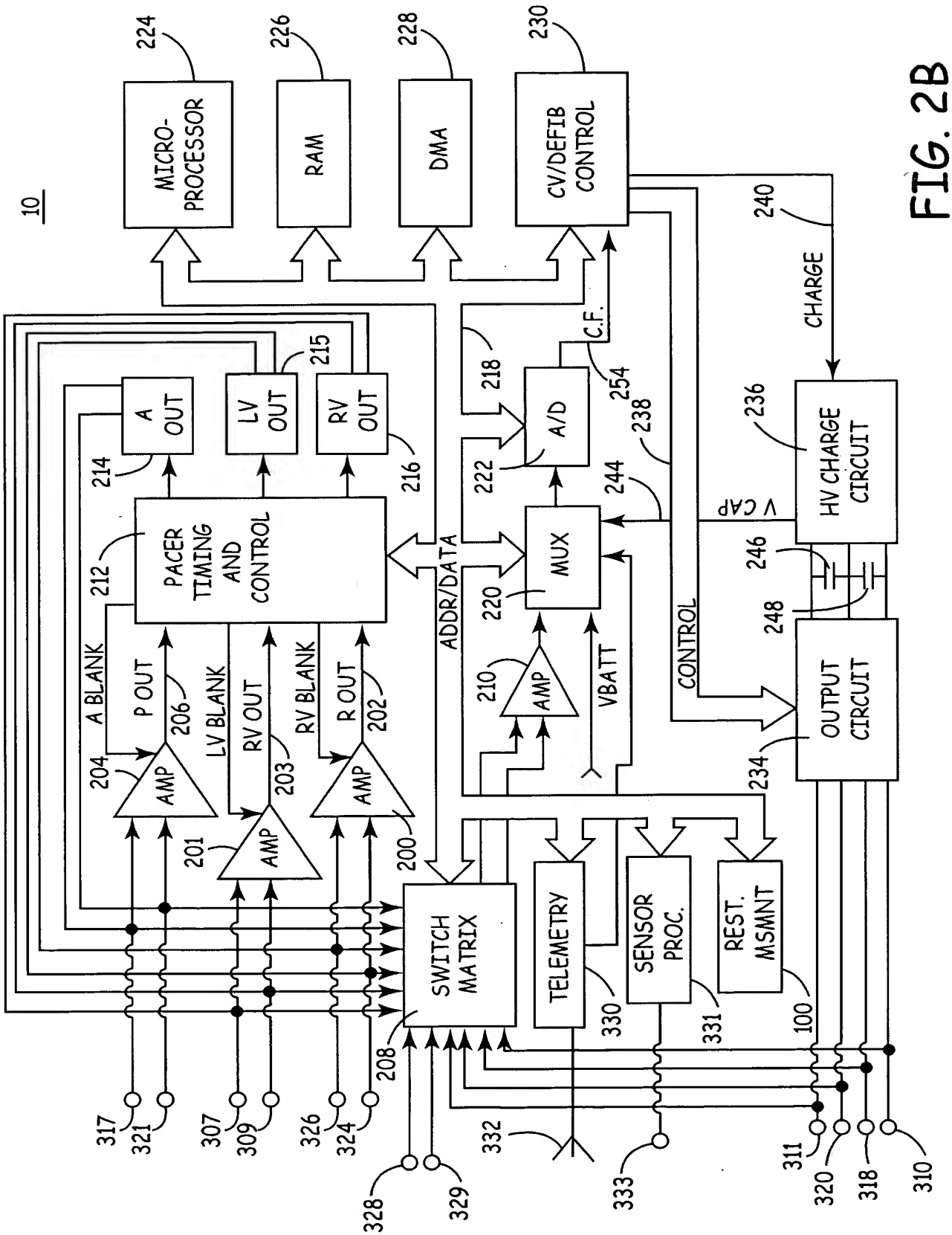
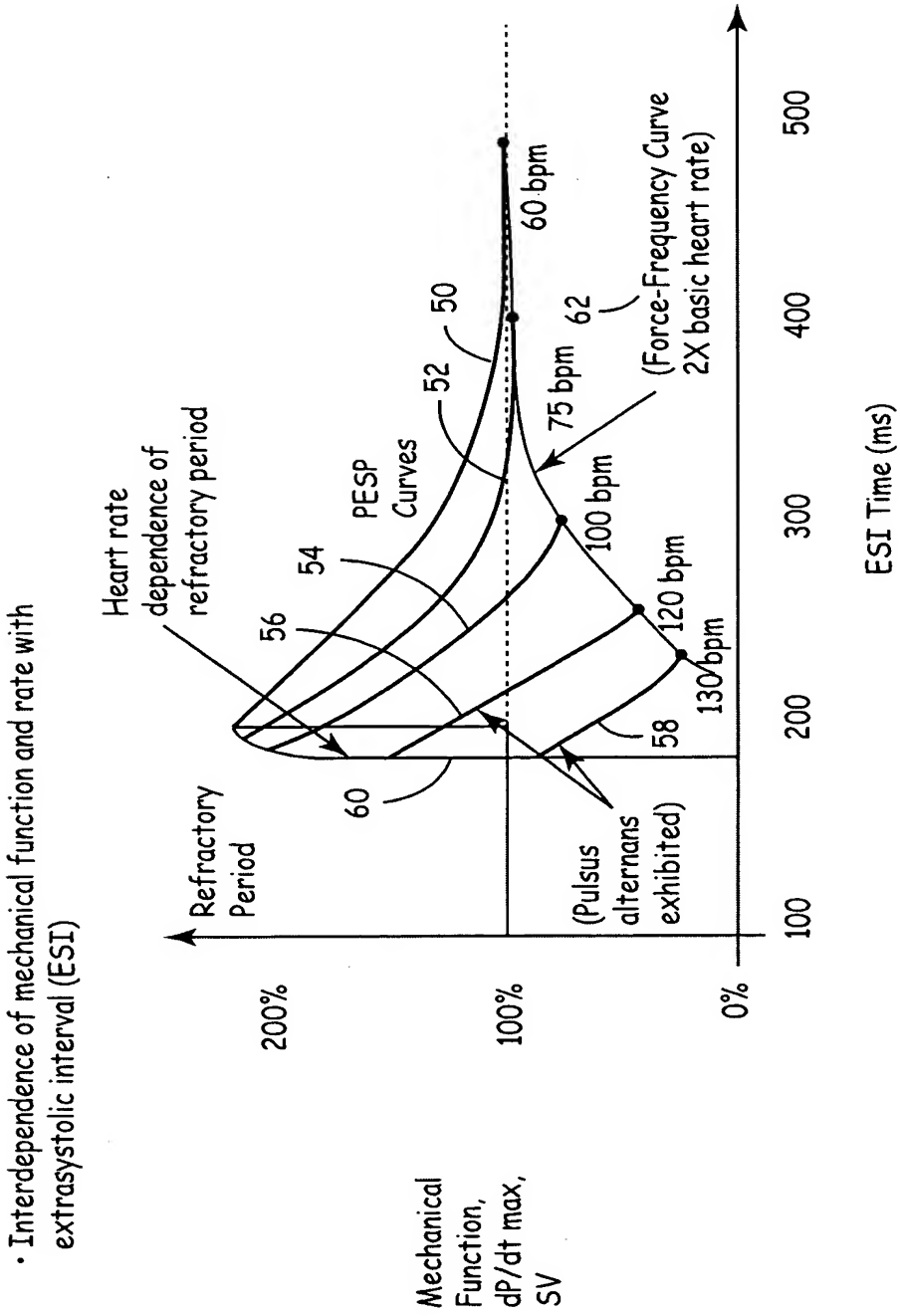

10
MICRO-PROCESSOR
224
RAM
226
DMA
228
CV/DEFIB CONTROL
230
240
CHARGE
C.F.
254
218
A/D
222
238
236
HV CHARGE CIRCUIT
V CAP
246
248
A OUT
214
LV OUT
215
RV OUT
216
PACER TIMING AND CONTROL
212
ADDR/DATA
MUX
220
244
A BLANK
P OUT
206
LV BLANK
RV OUT
203
RV BLANK
R OUT
202
AMP
204
AMP
201
AMP
200
AMP
210
VBATT
CONTROL
OUTPUT CIRCUIT
234
SWITCH MATRIX
208
TELEMETRY
330
SENSOR PROC.
331
REST. MSMNT
100
317
321
307
309
326
324
328
329
332
333
311
320
318
310

FIG. 2B

FIG. 3


• Interdependence of mechanical function and rate with extrasystolic interval (ESI)
Mechanical Function, dP/dt max, SV
200%
100%
0%
Refractory Period
100
200
300
400
500
ESI Time (ms)
Heart rate dependence of refractory period
PESP Curves
50
52
54
56
60
58
60 bpm
75 bpm
100 bpm
120 bpm
130 bpm
62
(Force-Frequency Curve 2X basic heart rate)
(Pulsus alternans exhibited)

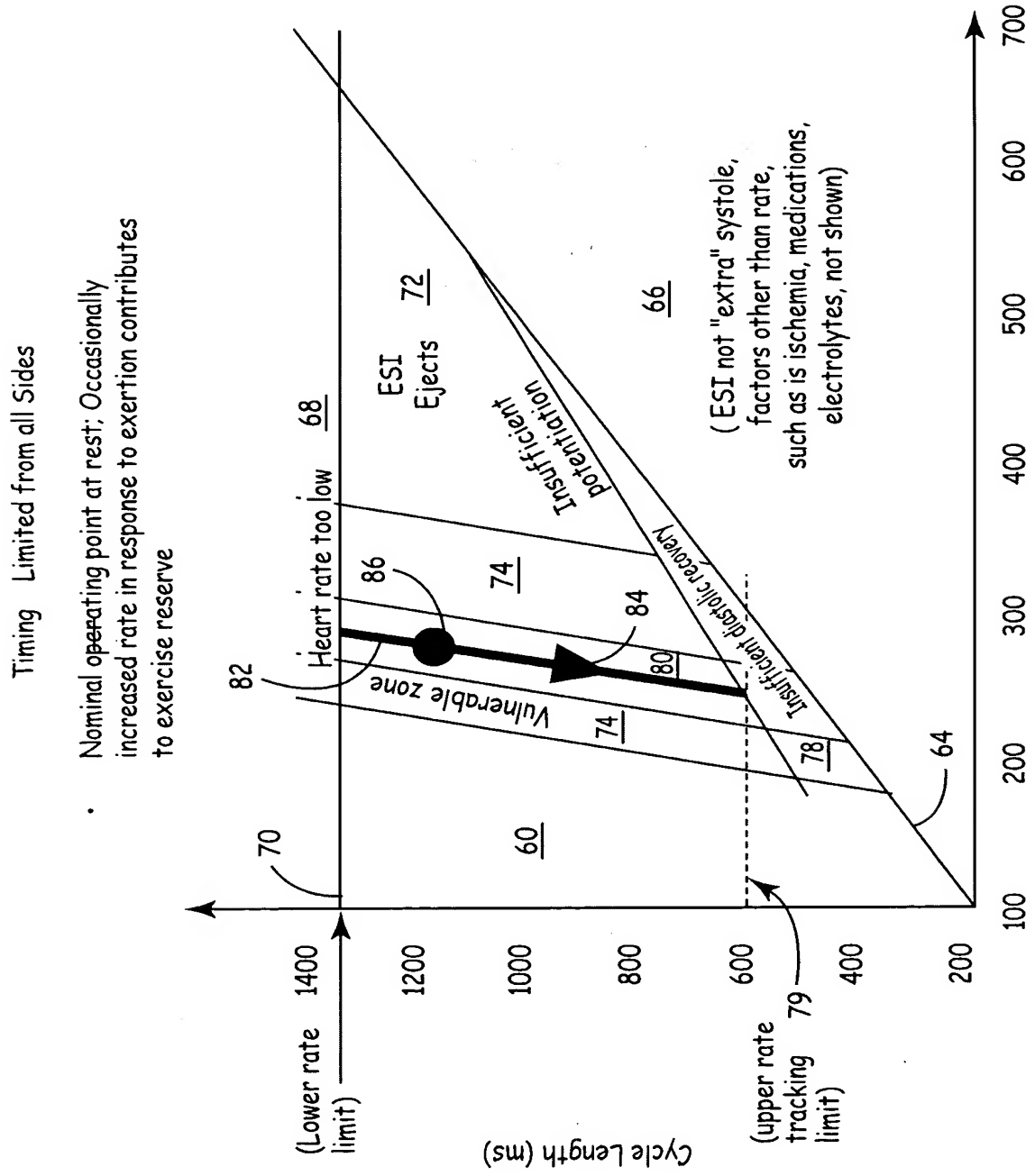
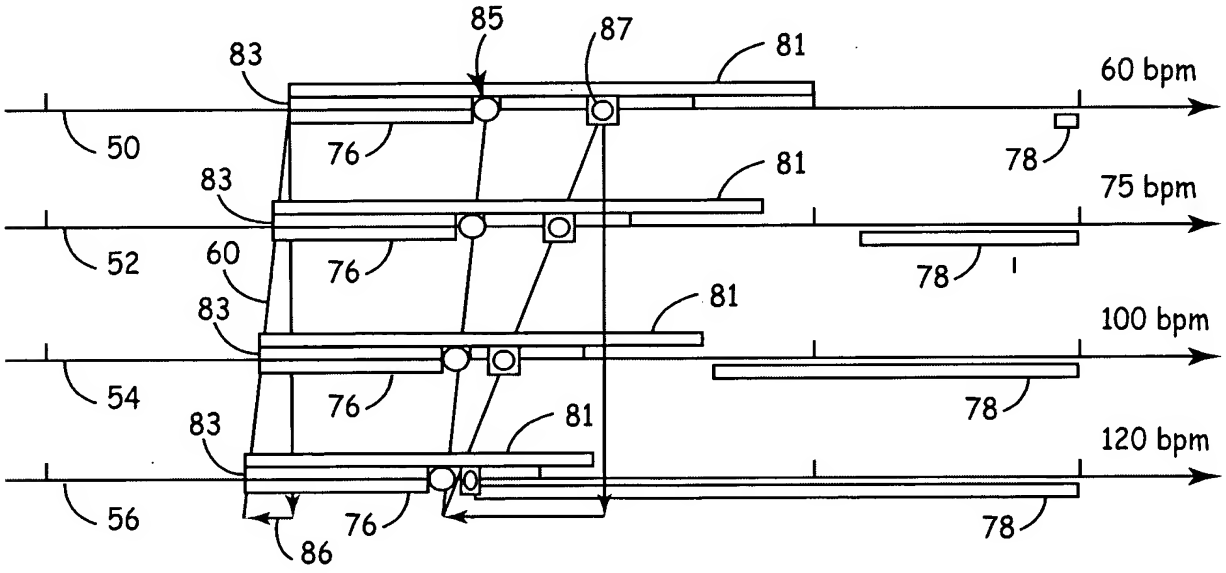

Timing Limited from all Sides
Nominal operating point at rest; Occasionally increased rate in response to exertion contributes to exercise reserve
Cycle Length (ms)
ESI (ms)
(Lower rate limit)
(upper rate tracking limit)
70
79
1400
1200
1000
800
600
400
200
100
200
300
400
500
600
700
60
66
68
ESI Ejects 72
Heart rate too low
82
86
74
84
80
74
Vulnerable zone
Insufficient diastolic recovery
Insufficient potentiation
78
64
(ESI not "extra" systole, factors other than rate, such as is ischemia, medications, electrolytes, not shown)

FIG. 4

Optimal ESI Timing and Heart Rate

- Sweet spot, balancing safety and effect, narrows and moves closer to refractory period as rate increases
- Upper rate limit necessary for CPT
- Adjustment of ESI with rate not necessarily identical to refractory or QT interval change with rate, depending on strategy and upper rate limit
- Importance of tracking refractory period



Optimally robust spot (87)
Excess risk: induced VT/VF (76)
Excess risk: paced Vcp tach (78)
Maximal benefit at fixed acceptable risk spot (85)
Benefit: hemodynamic, exercise capacity (81)
Benefit: rate lowering, reverse remodeling (83)

FIG. 5

FIG. 6

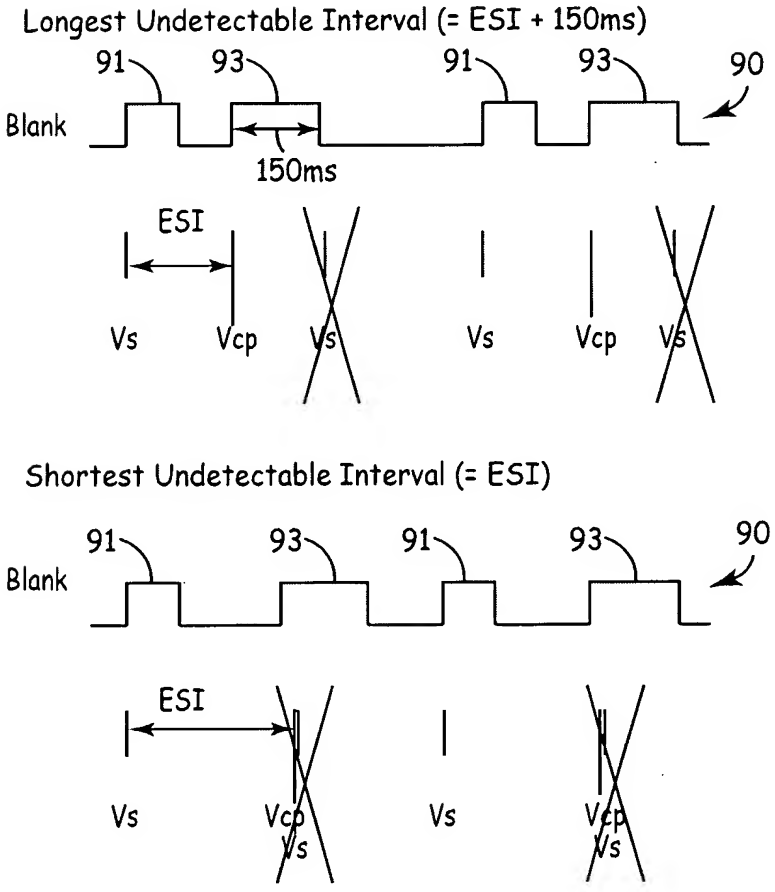

Longest Undetectable Interval (= ESI + 150ms)
91
93
91
93
90
Blank
150ms
ESI
Vs
Vcp
Vs
Vs
Vcp
Vs
Shortest Undetectable Interval (= ESI)
91
93
91
93
90
Blank
ESI
Vs
Vcp
Vs
Vs
Vcp
Vs

FIG. 7

Proposed Solutions

- Periodically drop ESS
  - Implementation of M of M+1 reveals VT after median delay of M/2 ESS cycles
  - Investigate reducing M at higher rates
  - Consider M = infinity (always on) if rate low enough. (m=0, always off, is already achieved at high rates via ESS rate limit safety rule.)
  - Can speed detection of VTs that are not 2:1 but are close and start with a phase that would otherwise delay their detection
- Suspend ESS upon inappropriate Asense timing
  - Safety rule engages with loss of AV synchrony during most VTs
- Dither timing of A-A or A-V intervals though A or V pacing
  - Occasional variations of 50-100 ms either way (if blanking is short) may be sufficient to enable hidden VT detection
- Auxiliary sensing vector
  - Use Coil-to-Can or other low polarization EGM signals to detect Vsense in blanking window
  - Discriminate by time or morphology from expected CPT evoked response
- Look for rate Irregularity as a clue to hidden VT
  - As VT rate enters/leaves undetectable VT zone, CPT rate will abruptly halve/double (perhaps exceeding upper rate limit)
- Reduce blanking/refractory
  - Moves left hand limit to the right (see diagram)
  - Incomplete solution by itself, since Vcp is intended to cause a prompt depolarization which needs to be blanked
  - Perhaps complete solution if implement electronic blanking of known time/morphology evoked R waves but not VTs (see auxiliary sensing vector note)
  - Two fold increase of change of R-R interval at base mechanical rate per change of blanking significantly adds to heart rate range over which VTs can be detected without dropping ESS beats
  - In principle, atrial cross chamber blanking can be made short enough (a few ms) to never hide a VT
  - Could be accomplished with low polarization leads or sense amp electronics modifications.
  - May be combined with auxiliary sensing vector solution
- Deliver ESS with short ESI
  - Enhances window for VT detection (particularly at a low ESS rates)
- Keep ESS upper rate limit low
  - Caps aliased VT rates. Upper limit 75 bpm makes all VTs faster than nominal VTDI detectable
  - Exploit in conjunction with reducing blanking and short ESIs (see above) to be least restrictive
  - Use an appropriately lower rate limit if Vpacing and not Vsensing to account for propagation differences.

FIG. 8

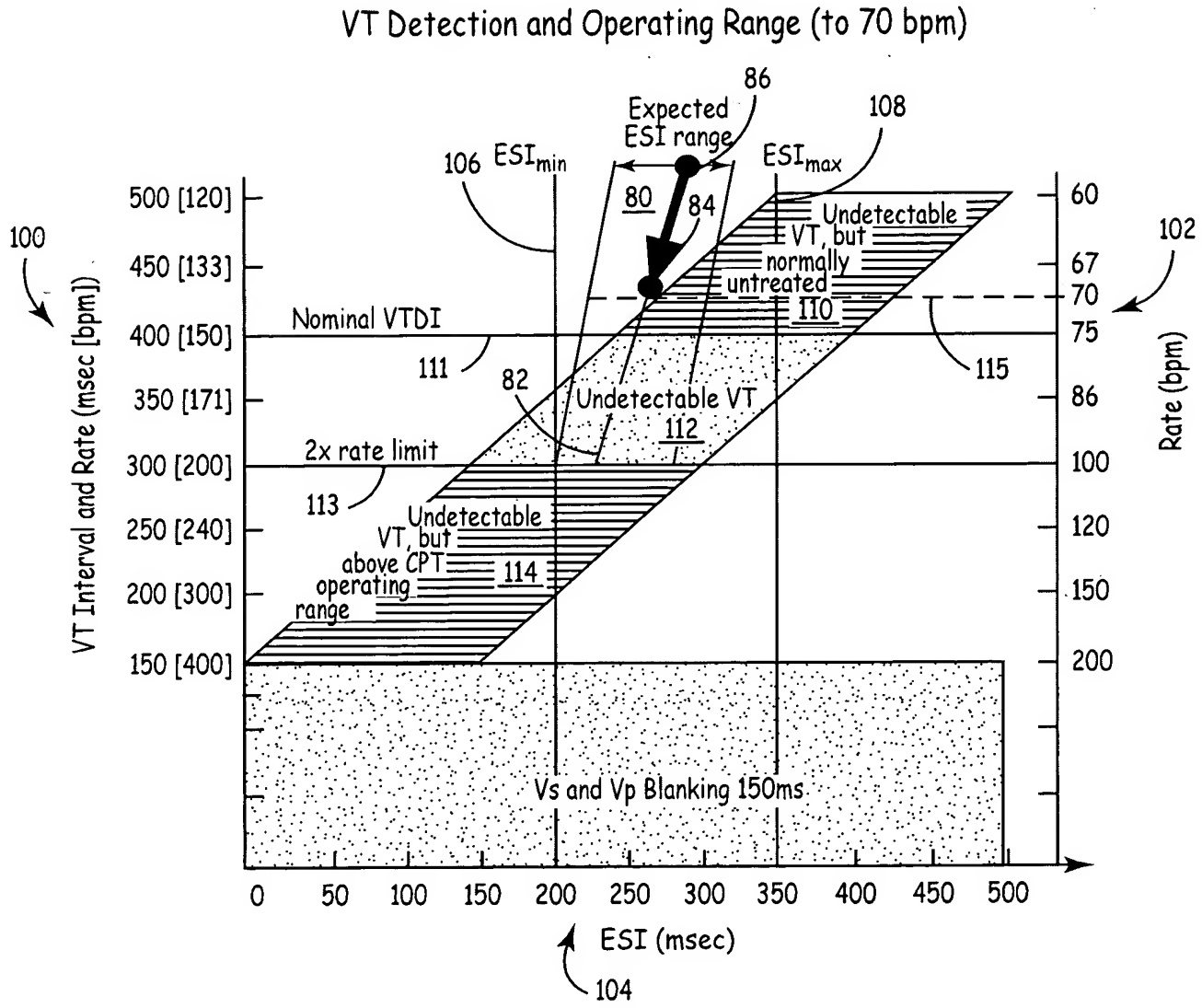

VT Detection and Operating Range (to 70 bpm)
86
Expected ESI range
108
106 ESI$_{min}$
ESI$_{max}$
80
84
100
102
500 [120]
450 [133]
400 [150]
350 [171]
300 [200]
250 [240]
200 [300]
150 [400]
60
67
70
75
86
100
120
150
200
Undetectable VT, but normally untreated
110
Nominal VTDI
111
115
82
Undetectable VT
112
2x rate limit
113
Undetectable VT, but above CPT operating range
114
VT Interval and Rate (msec [bpm])
Rate (bpm)
Vs and Vp Blanking 150ms
0 50 100 150 200 250 300 350 400 450 500
ESI (msec)
104

FIG. 9

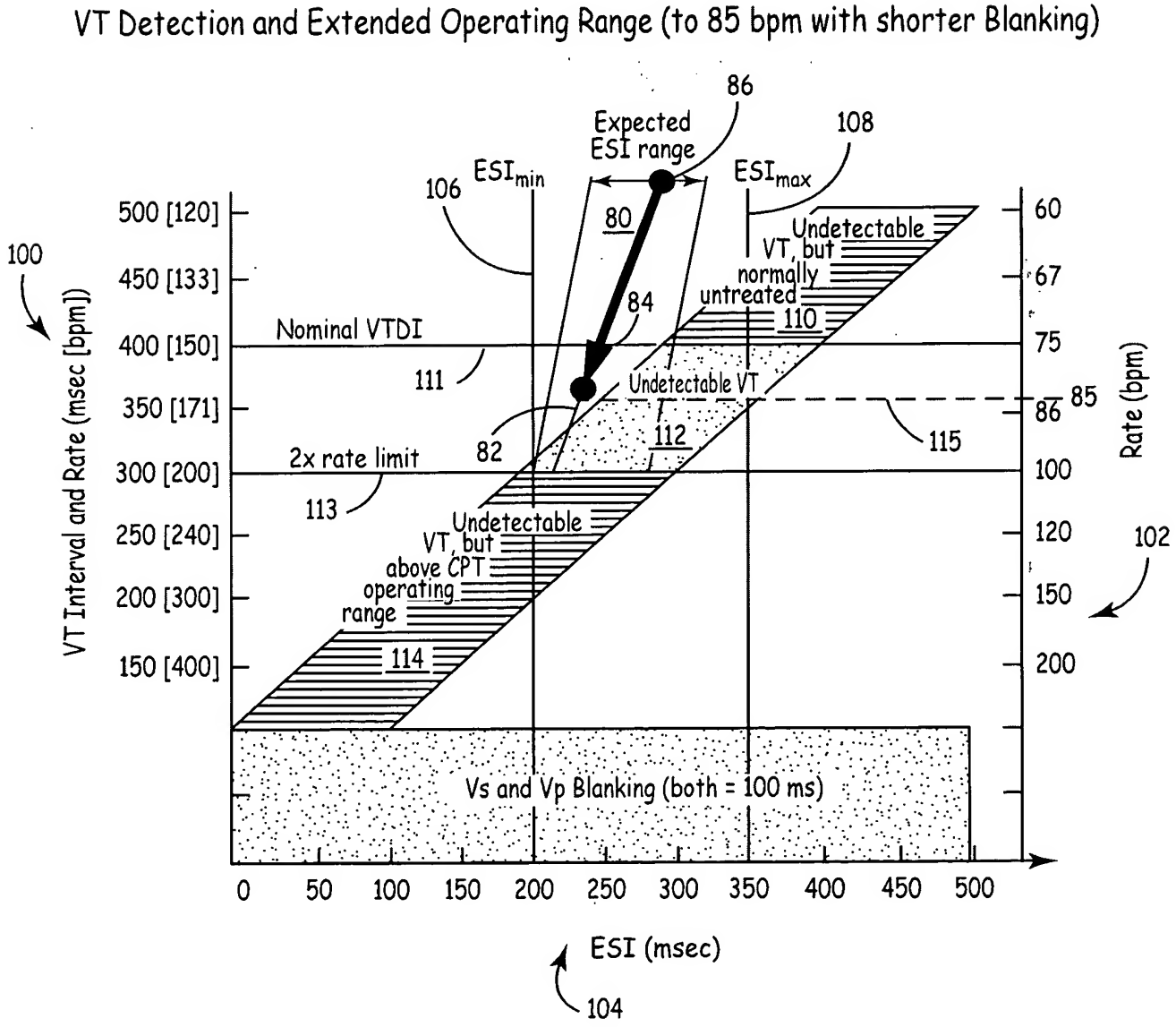

VT Detection and Extended Operating Range (to 85 bpm with shorter Blanking)
100
VT Interval and Rate (msec [bpm])
500 [120]
450 [133]
400 [150]
350 [171]
300 [200]
250 [240]
200 [300]
150 [400]
Nominal VTDI
2x rate limit
Expected ESI range
86
108
106
ESI$_{min}$
ESI$_{max}$
80
84
82
111
113
Undetectable VT, but normally untreated
110
Undetectable VT
112
115
Undetectable VT, but above CPT operating range
114
Vs and Vp Blanking (both = 100 ms)
60
67
75
85
86
100
120
150
200
Rate (bpm)
102
0
50
100
150
200
250
300
350
400
450
500
ESI (msec)
104

FIG. 10

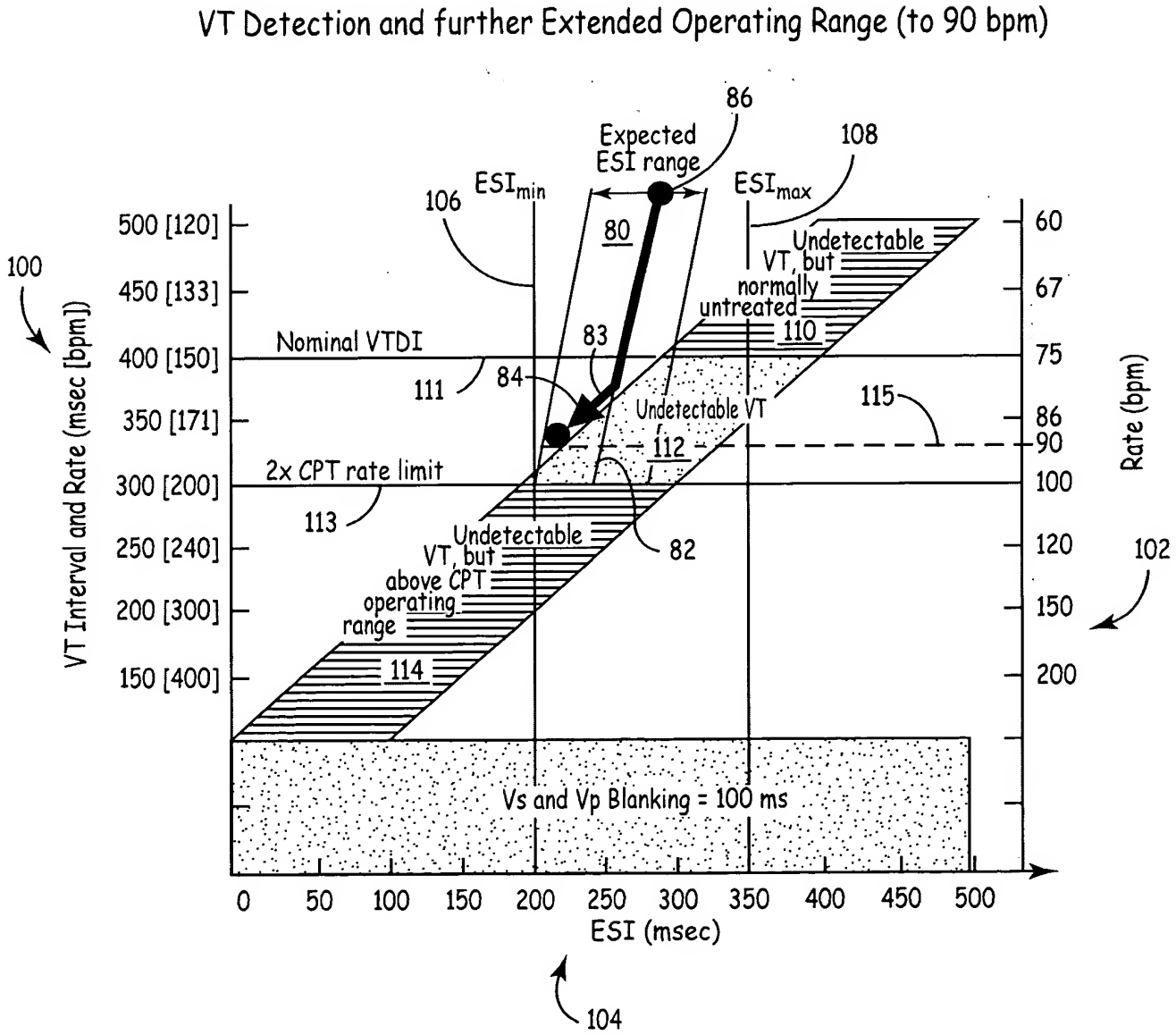

VT Detection and further Extended Operating Range (to 90 bpm)
100
86
Expected ESI range
108
ESI$_{min}$
ESI$_{max}$
106
80
Undetectable VT, but normally untreated
110
83
Nominal VTDI
111
84
Undetectable VT
115
112
2x CPT rate limit
113
82
Undetectable VT, but above CPT operating range
114
Vs and Vp Blanking = 100 ms
500 [120]
450 [133]
400 [150]
350 [171]
300 [200]
250 [240]
200 [300]
150 [400]
VT Interval and Rate (msec [bpm])
60
67
75
86
90
100
120
150
200
Rate (bpm)
102
0
50
100
150
200
250
300
350
400
450
500
ESI (msec)
104

FIG. 11

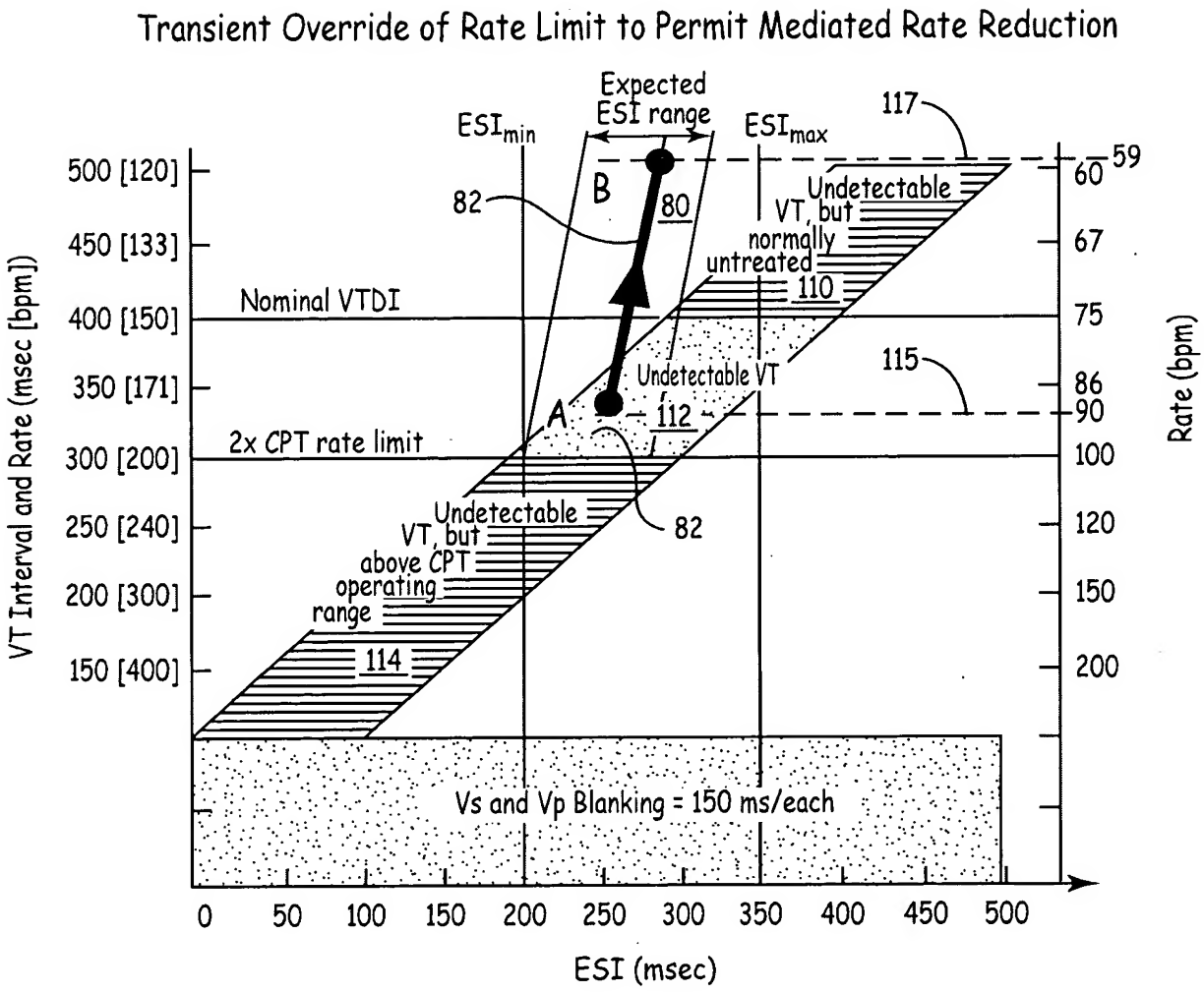
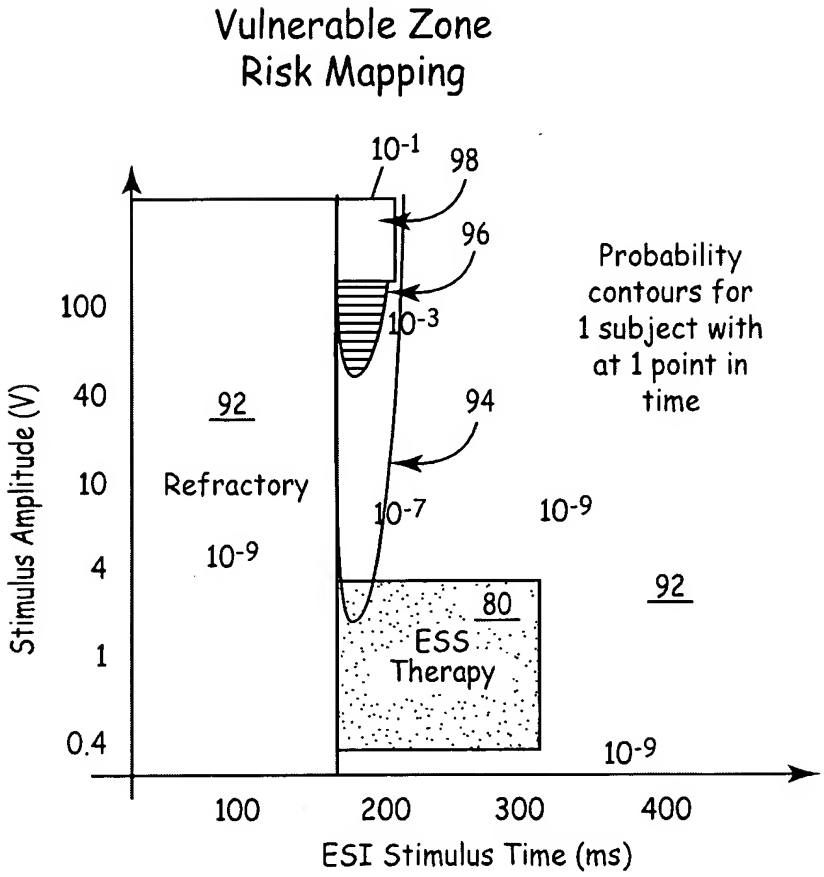

Transient Override of Rate Limit to Permit Mediated Rate Reduction
Expected ESI range
ESI$_{min}$
ESI$_{max}$
117
B
82
80
Undetectable VT, but normally untreated
110
Nominal VTDI
Undetectable VT
115
A
112
2x CPT rate limit
82
Undetectable VT, but above CPT operating range
114
Vs and Vp Blanking = 150 ms/each
500 [120]
450 [133]
400 [150]
350 [171]
300 [200]
250 [240]
200 [300]
150 [400]
VT Interval and Rate (msec [bpm])
60
59
67
75
86
90
100
120
150
200
Rate (bpm)
0
50
100
150
200
250
300
350
400
450
500
ESI (msec)

FIG. 12


Vulnerable Zone
Risk Mapping
10-1
98
96
10-3
94
10-7
10-9
92
Refractory
10-9
80
ESS
Therapy
92
10-9
Probability
contours for
1 subject with
at 1 point in
time
Stimulus Amplitude (V)
100
40
10
4
1
0.4
100
200
300
400
ESI Stimulus Time (ms)